REMARKS/ARGUMENTS

Claims 1-3 and 5-19 are active and are drawn to the elected subject matter. Claims 20-65 have been cancelled in view of the finality of the Restriction Requirement imposed by the Office.

The specification is amended to include symbols that are obvious from the Figures submitted with the application when it was filed.

Support for the amendment to Claim 1 is found in Claim 4 and the specification on page 10, lines 17-19. The remaining claim amendments are made for clarity and to provide proper antecedent basis in view of the amendment to Claim 1. The objections and rejections under 35 U.S.C. § 112, first and second paragraphs are obviated by the submitted amendments.

No new matter is added.

The sole remaining issue from the Office Action is the rejection of Claims 1-6, 18 and 19 under 35 U.S.C. § 103(a) in view of Martiniuk et al, Stanley, Bijvoet, Fuhrmann, and Elbein. This rejection is not sustainable because the combination of publications does not provide the requisite suggestion that the method as claimed, which pertains to the production of lysosomal hydrolases, would be required as opposed to some other method of producing a lysosomal hydrolase with high mannose oligosaccharides.

Applicant states on page 2, lines 12-14: "Lectin resistant cell lines, in general, are known (Stanley (1983) Meth. Enzymology 96:157-189; Gottlieb et al (1974) Proc. Nat. Acad. Sci., U.S.A., 71(4):1078-1082; Stanley et al (1990) Somat Cell Mol Genet (3):211-223)."

In addition on pages 3-4, the Applicant describes again that lectin resistant cell lines were known and therefore to produce a lysosomal hydrolase with reduced complex carbohydrates, one could use a known lectin resistant cell line and introduce a expression vector carrying the polynucleotide that would encode the lysosomal hydrolase.

In fact, expression of a protein in a pre-existing lectin resistant cell line is the common protocol in the field as shown by the representative 10 Abstracts attached hereto, which were obtained from the PubMed database.[1]

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[1] Parcyk (FEBS Lett. 1991 278(2):267-70) describes the expression of a viral glycoprotein in lectin resistant Madin-Darby canine kidney (MDCK) cells. Hughes and Mills (J Cell Physiol 1996, 128(3):402-12) describes the expression of various glycoproteins in lectin resistant Baby hamster kidney) BHK cells. Yu et al (Mol Genet Metab. 2000, 71(4):573-80) describes the production of the lysosomal enzyme alpha-N-acetylglucosaminidase (involved in Sanfilippo syndrome type B) in lectin resistant Chinese Hamster Ovary (CHO) cells. Carbonneau and Stanners (Cell Adhes Commun. 1999, 7(3):233-44) describes the production of human carcinoembryonic antigen (CEA) in lectin resistant CHO cells. Nagayama et al (J Biol Chem. 1998, 273(50) :33423-8) describes the production of tyrotropin receptor in lectin resistant cells. Fuller et al (Biochim Biophys Acta, 1998, 406(3):283-90) describes the production of the lysosomal enzyme N-acetylgalactosamine-4-sulphatase (involved in Mucopolysaccharidosis type IV) in lectin resistant CHO cells. Fenouillet et al (Virology, 1996, 218(1):224-31) describes the production of HIV membrane glycoproteins in lectin resistant CHO cells. Grossman et al (J Biol Chem, 1995, 270(49):29378-85) describes the expression of thyrotropin in lectin resistant CHO cells. Haspel et al (J Cell Physiol, 1988, 136(2):361-6) describes the expression of hexose transporter glycoprotein in lectin resistant CHO cells. Koyama and Hughes (J Biol Chem, 1992, 267(36):25939-44) describes the expression of integrins in lectin resistant BHK cells.

As further discussed on page 4, lines 3-13:

> However, in attempts to transform a lectin resistant cell line in order to express a non-native glycoprotein, e.g., acid α-glucosidase, the amount of protein expressed and thus recovered was very poor thereby having little practical utility.
>
> The present inventors have discovered quite unexpectedly that when a mammalian cell is transfected to express a glycoprotein of interest is subjected to lectin selection, one is able to obtain both high levels of glycoprotein expression coupled with a reduction in complex carbohydrates on the glycoproteins' surface are observed.

The present claims provide introducing the polynucleotide encoding the lysosomal hydrolase and then culturing the transfected cell with a lectin to obtain a lectin resistant cell which expresses the lysosomal hydrolase. Therefore, the order in which the steps of the claimed method are performed were found to be important for producing a lysosomal hydrolase with reduced complex carbohydrates practicable. The lack of success in producing a lysosomal hydrolase by transfecting a lectin resistant cell is described in the application on page 4, which is also reproduced above. The success of producing lysosomal hydrolases according to the claimed method is demonstrated in the Examples section of the present application, see pages 23-26.

As the cited prior art provides no description or suggestion that the order in which the introducing and selecting must be performed when producing a lysosomal hydrolase with high mannose oligosaccharides, the claims would not have been obvious. Furthermore, the fact that transfecting a lectin resistant cell did not work relative to the claimed method demonstrates that the present claims would not have been obvious. Therefore, withdrawal of this ground of rejection is requested.

Allowance of this case is requested.

Respectfully submitted,

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